AUA
Association of University Anesthesiologists
Update
Summer 2014

CONTENTS

AUA President's Panel at 2014 AUA Annual Meeting: Genomics, Big Data, and Publication Pitfalls

W. Andrew Kofke, M.D., M.B.A., F.C.C.M.
University of Pennsylvania
AUA Update Editor

A most provocative President's Panel dealing with genomics, big data, and publication pitfalls was held and moderated by AUA Immediate Past President, Dr. Lee Fleisher.

Michael Snyder, M.D., FACS, Professor and Chair of Genetics and Director of the Stanford Center for Genomics and Personalized Medicine, presented a lecture titled "Genomics and Personalized Medicine."

His talk started with a declaration that health is a product of genome and environment. He referred the audience to the movie *Gattaca* as a relevant metaphor for a potential future. He pointed out that the cost of DNA sequencing is plummeting. He went on to talk about the impact of genomics in medicine, including (1) to understand and treat disease, (2) pharmacogenomics driving drug therapy, and (3) managing health care in healthy people.

It is now clear that cancer is a genetic disease with some 10-20 driver mutations unique to each cancer. Determination of these driver mutations will provide a logical path to effective personalized therapy of each type of cancer. As an example he described a patient with metastatic colon cancer. He had spikes in EDGR and CDK6 and this sequence led to unique therapy based on genomics. Another example is using genomics to solve mystery diseases in children. He presented examples where genomics lead to a diagnosis otherwise not identifiable.

Then he went on to discuss personal genome sequencing in healthy people. This will include personal "omics" profiling. This will include development for possibly billions of individuals' characterization of the genome, epigenome, transcriptome, proteome, cytokine-ome, metabolome, auto antibody-ome, and microbiome (gut, urine, nose, tongue, and skin). With this we will have lots of impressively big data (e.g., a million genes and other –omic information in millions and billions of people). One hoped-for consequence of this will be an ability to predict disease and monitor diseases. This should lead to new therapeutic strategies for diseases.

He provided a graphical example of this approach in describing his own genome, collected through 6 viral infections. His initial genomic evaluation indicated a risk of basal cell ca, glaucoma, hyperlipidemia, macular degeneration, degenerative joint diseases, and diabetes mellitus. Notwithstanding his lean habitus, he did indeed recently develop diabetes mellitus and is monitoring it with his various omic profiles…all of course coordinated with his primary care provider.

Notably his genome, based on pharmacogentic knowledge, predicts his response to statins and to various oral diabetic meds, information he is using to guide his therapy.

He reported that genome sequencing is poised to be translated to impact clinical medicine. He envisions a world where genomic and other -omic information is derived at birth from each person, who at that early time will have a unique –omics profile which will then be used to predict and prevent disease, monitor disease progress, and guide treatment. More information can be found at snyderome.stanford.edu.

The next talk was by Jure Leskovic, B.Sc., Ph.D., Assistant Professor of Computer Science at Stanford, on "What Big Data Can Teach Us About Human Behavior." He began his presentation by discussing the rich and dynamic interactions which arise and can be observed between millions of computer and device users and the sites with which they interact.

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Genomics, Big Data, and Publication Pitfalls

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This then leads to massive digital traces of human activity and creates the situation where the web has become our laboratory for understanding the pulse of humanity. What was previously invisible has become visible. Notwithstanding any issues with privacy and so on, he asserted that this is a situation where the science of population-based human behavior is poised to advance. He reviewed the concept that the many digital traces lead to networks between people and between communities. Indeed, he suggests that to make progress we need to develop a new branch of mathematics, computer science theory, graph theory, computing platforms and algorithms for data mining and machine learning.

He presented examples of using such data to determine how people become members of communities and how language develops within communities and within individuals and changes over time. He also discussed how such approaches have shown how people respond to various incentives and thus how such big data can be used to steer human behavior. He presented a figure that looked like a vector demonstrating this new area of badge theory applied to modify innate behavior to something between desired and innate behavior.

Dr. Snyder presented the lecture, "Genomics and Personalized Medicine."

The 2014 President's Panel addressed genomics, big data and publication pitfalls.

John Ioannidis, M.D., the CF Rehnborg Professor in Disease Prevention in the School of Medicine and Professor of Health Research and Policy at Stanford, presented a lecture on "Pitfalls in the Analysis of Published Data." He began with the observation that there are 15 million different scientists publishing their data all over the world. One consequence of this is over rich databases which when overanalyzed can yield erroneous conclusions. One example he provides is an analysis of 559 classes of drugs used in virtually every patient in Sweden. This analysis indicates that 75% of all drugs can have an effect on the development of cancer. He describes this as a pitfall of too much data inappropriately analyzed.

He suggests that there is a need to register all observational databases, describing five levels of database types.

He then went on to discuss the importance of public availability of data used to write scientific papers. He noted that there is a requirement for public availability of published research data in high impact journals. However, under scrutiny he reports that very few actually adhere to the policy.

Many analyses are very data rich. It is quite difficult for an outsider to reanalyze data. He did a study looking at attempts by teams to duplicate published data from a very high impact journal. Over half could not be reproduced due to unclear data, homemade software, or unclear methods.

He also discussed reanalysis of data from RCTs. The example discussed was the Tamiflu meta analysis wherein reanalyzing the raw data yields totally different conclusions. He indicated that most studies claiming to be a reanalysis aren't really. Most are the same investigators and only 36% tested the very same hypotheses. Notably almost half of the reanalyses reached different conclusions.

He discussed the Center for Open Science, an initiative based in psychology which is trying to reproduce the most highly cited papers.

He promises that he can create any result you want with a database.

He then went on to critique metaanalyses specifically discussing what we have learned from 85,000 meta-analyses in the Cochrane database.

How many therapies do we have that are extremely effective and decrease mortality >5x? He notes that penicillin, insulin, and CPR arguably are in this high efficacy category but none have undergone randomized controlled trials. ECMO is effective in babies and that's about it. He went on to point out that initial reports of large effect estimates deflate on subsequent studies.

He discussed the geometry of trial networks for neglected tropical diseases which affect about 1 billion people. Unfortunately he asserts that one cannot make sense of a single trial and that most treatment comparisons of interest have never been addressed.

He also mentioned the problem of overlapping metaanalysis on the same topic (e.g., use of statins after cardiac surgery). All found the same results, and he suggests that this constitutes a waste of effort.

He then discussed the need for international large scale collaboration and agreements to combine data from big data sets. The world is changing. Soon China will be publishing more English language papers than the United States. However, he asserts that they will not be reliable conclusions in the absence of big data sets from consortia of investigators.

AUA 61st Annual Meeting at Stanford University

More than 250 members and guests of the Association of University Anesthesiologists gathered together for the AUA 61st Annual Meeting, April 24-26, at Stanford University School of Medicine, Stanford, California, to exchange new ideas and develop new methods for teaching anesthesia. The Annual Meeting Planning Committee, led by Dr. Ronald G. Pearl, Dr. Charles W. Emala, and Dr. David J. Murray, developed a robust educational and scientific program including sessions focused on lung injury, remodeling and repair, the effectiveness of the classroom model, original investigations in the clinic and laboratory, and oral presentations highlighting award winners.

Announcing the AUA 61st Annual Meeting Award Winners

The following 2014 abstract award winners were recognized for their valuable contribution to the subspecialty of academic anesthesiology and for their outstanding scientific research and oral presentation at the AUA 61st Annual Meeting.

Margaret Wood Resident Research Award Winner

Postoperative Dementia: Role of Anesthesia and APOE4

Katie J. Schenning, M.D., M.P.H.
Oregon Health & Science University
Portland, Oregon

Junior Faculty Award Winners

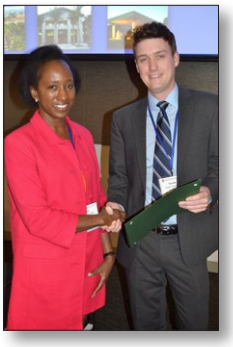
Inflammation Increases Brain Sensitivity to General Anesthetics

Sinziana Avramescu, M.D., Ph.D., F.R.C.P.C.
Sunnybrook Health Sciences Centre
Toronto, Ontario, Canada

Specialized Pro-Resolving Mediators in a Mouse Model of Postoperative Cognitive Decline

Niccolò Terrando, B.Sc (hons), D.I.C., Ph.D.
Karolinska Institute
Stockholm, Sweden

Resident Travel Award Winners



Genetic Deletion of the GABA-A alpha4 Subunit Leads to Increased Airway Resistance and Inflammation

Gene T. Yocum, M.D.
Columbia University
New York, New York

miR-200c Contributes to Injury from Transient Cerebral Ischemia in Mice by Targeting Reelin

Creed M. Stary, M.D., Ph.D.
Stanford University
Stanford, California

EAB Report: 2014 AUA Annual Meeting

David J. Murray, M.D.
Immediate Past Chair,
Educational Advisory Board
Professor of Medicine
Director, Howard and
Joyce Wood Simulation Center
Washington University School of Medicine

The AUA's Education Advisory Board sponsored two panels on Friday morning at the 2014 AUA Annual Meeting in Palo Alto.

Educational Research and Education Career Outcomes: Anesthesiology Education Grants

The first panel moderated by Cathy Kuhn, M.D., Associate Dean for Graduate Medical Education at Duke University, was entitled, "Educational Research and Education Career Outcomes: Anesthesiology Education Grants." The session began with Dr. Kuhn's overview of the FAER programs including the FAER Academy of Education Mentors in Anesthesiology. Dr. Kuhn provided details about the Research in Education Grant funding mechanism. The four other panelists described their research, their research outcomes as well as the impact of the award on their careers.

Edward R. Mariano, M.D., MAS (Clinical Research), Associate Professor of Anesthesiology at Stanford University, described the preliminary results from his research in education project entitled, "An Efficacy Study of Simulation-Based Training on Practicing Anesthesiologists' Acquisition of Ultrasound-Guided Perineural Catheter Insertion Skills." The project, funded by FAER in 2012, was designed to determine whether an educational intervention directed at practicing anesthesiologists could improve not only their skill in regional anesthesia but whether these skills would lead them to provide ultrasound-guided regional anesthesia techniques for their patients.

> *"This was followed by a simulation-based intervention project which was based in adult learning theory and demonstrated measurable improvements in 'speaking up' language. Two years later, participants were shown to have better abilities to speak up when compared to naive controls."*

Santhanam Suresh, M.D, FAAP, Education Grant Recipient 2008, described the project, "Regional Anesthesia Education in Infants: A Novel Computer Based Visual Learning Technique to Improve Confidence and Performance in Anesthesia Residents." Dr. Suresh's project applied a visual learning methodology for novice residents to learn caudal anesthesia. The preparation improved residents' clinical performance as measured by faculty members in an operating room setting. The approach has general applicability for other procedures and is now incorporated into the resident curriculum at Ann & Robert H. Lurie's Children's Hospital of Chicago.

May Pian-Smith, M.D., M.S., from Harvard Medical School and Massachusetts General Hospital, described her project entitled "Teaching Residents to Question and Challenge: An Experiential Approach." This work included a needs assessment phase to determine factors which act to self-censor trainees so that they do not "speak up" across authority gradients about issues related to patient safety. This was followed by a simulation-based intervention project which was based in adult learning theory and demonstrated measurable improvements in "speaking up" language. Two years later, participants were shown to have better abilities to speak-up when compared to naive controls. Dr. Pian-Smith was co-investigator on an APSF grant and has subsequently developed "speaking up" programming for interdisciplinary teams of trainees and faculty. Her talk concluded with a discussion of the importance of mentoring in the career development of researchers in education.

Dr. Kuhn moderated the EAB Program (Part 1): "Research and Research Career Outcomes: Anesthesiology Education Grants."

The fourth panelist, David Murray, M.D., from Washington University in St Louis, described the findings from a 2005 FAER Research in Education grant entitled, "Acute Care Skills in Anesthesia Practice: A Simulation-Based Performance Assessment." Dr. Murray described how a multiple-scenario simulation methodology was used to develop a valid and reliable performance assessment for anesthesia practice. This initial project funded by FAER led to three subsequent grants from the Agency for Health Quality and Research (AHRQ) that applied a similar multiple scenario simulation methodology to assess competence in medical students beginning internship, pediatric residents in critical care settings as well as to study the teamwork skills of trauma and pediatric rapid response teams.

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EAB Report

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EAB Program (Part 2) addressed "Evidence, Economics, and Outcomes in the Educational Methodology: Is Face-to-Face Learning in a Classroom Model Obsolete?"

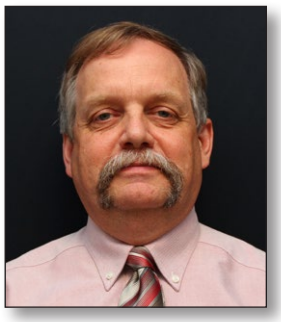
Dr. Chu discussed new strategies for delivering educational content.

Evidence, Economics, and Outcomes in Educational Methodology: Is Face-to-Face Learning in a Classroom Model Obsolete?

The second EAB panel was titled "Evidence, Economics, and Outcomes in Educational Methodology: Is Face-to-Face Learning in a Classroom Model Obsolete?" In advance of the AUA Annual Meeting, a survey of the AUA membership was developed by the panelists and Amy DiLorenzo, M.A. (University of Kentucky) that queried AUA members about their current practice and their perception of evidence for various modes of delivery of educational content. Randy Schell, M.D., from the University of Kentucky, defined the traditional classroom model in which students read textbooks outside of the classroom and attend class for lectures and tests. He presented the AUA membership survey results and evidence for moving passive lectures outside of the traditional classroom to an on-line format and for using class time for more active learning methods. The advantages and evidence for blended learning (on-line plus face-to-face class time) including "flipped classroom" was presented. Manny Pardo, M.D., from the University of California, San Francisco, blended historical and extremely insightful quotes about anesthesiology education from Stuart Cullen, with current evidence for blended learning. He described the forces encouraging change in the way we deliver educational content (i.e. duty hours, clinical workload, generational differences in preferences for learning), economic issues in delivery of educational content, and evidence from a large metaanalysis study from the US Department of Education, demonstrating that online learning is as effective as classroom instruction but blending on-learning with face-to-face instruction had even stronger learning outcomes than did face-to-face instruction alone. Larry Chu, M.D., M.S., from Stanford University, concluded the panel with a discussion of new strategies for delivering educational content that are well received by a newer generation of learners. He focused on the practical implementation of the previously discussed topics including methods to leverage technology for the benefit of teachers and learners. The question proposed by Prober and Heath in their editorial piece entitled, "Lecture Halls Without Lectures" (N Eng J Med 2012), "Why would anyone waste precious class time on a lecture," was used to help initiate a discussion with audience participation that concluded the EAB Panel.

"He focused on the practical implementation of the previously discussed topics including methods to leverage technology for the benefit of teachers and learners."

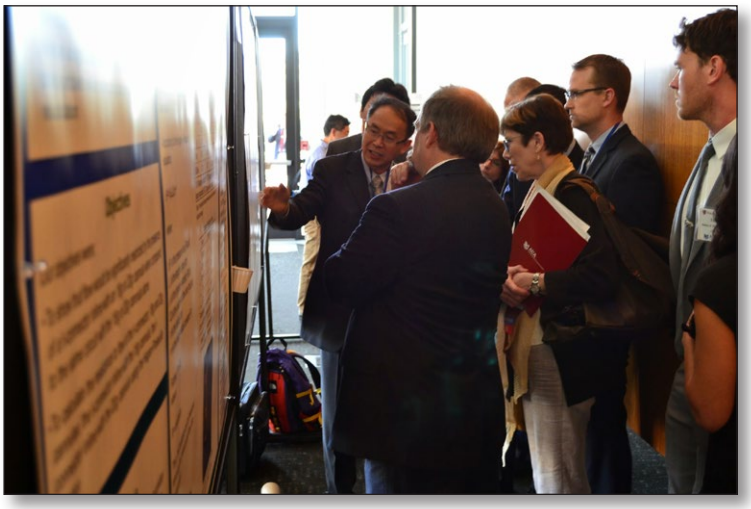
SAB Report of 2014 AUA Annual Meeting



Charles W. Emala, M.D., Chair
Scientific Advisory Committee
Columbia University

The Scientific Advisory Board (SAB) organized three oral sessions and two moderated poster discussion sessions at the 61st Annual Meeting of the AUA hosted by the Department of Anesthesiology of Stanford University at the Li Ka Shing Center for Learning and Knowledge on the campus of Stanford University. A mini-symposium on lung injury and repair was sponsored by the *American Journal of Physiology: Lung Cellular and Molecular Physiology* and was moderated by its editor-in-chief, Sadis Matalon, Ph.D. This mini-symposium was led by a superb keynote talk by Charles Serhan, Ph.D., in which the novel discovery of resolvins was presented. Three physician-scientist anesthesiologists then presented their interesting research programs in lung injury, repair and regeneration and this mini-symposium is reviewed in more detail in a separate section of this newsletter. The two traditional oral sessions each included 8 short talks and included two presentations by winners of the junior faculty award and three presentations by resident research awardees, including the newly endowed Margaret Wood, Resident Research Award. The first junior faculty awardee was Sinziana Avramescu, M.D., Ph.D., from Sunnybrook Health Sciences Center in Toronto for her talk entitled, "Inflammation Increases Brain Sensitivity to General Anesthetics." The second junior faculty awardee was Niccolò Terrando, B.Sc., Ph.D., from the Karolinska Institute in Stockholm for his talk entitled "Specializing Pro-Resolving Mediators in a Mouse Model of Postoperative Cognitive Decline." The inaugural Margaret Wood Resident Research Award, established to inspire and recognize original resident research was awarded to Katie Schenning, M.D., M.P.H., from Oregon Health and Science University for her talk entitled, "Postoperative Dementia: Role of Anesthesia and APOE4." The two resident travel awardees were G. Tom Yocum, M.D., of Columbia University for his talk entitled, "Genetic Deletion of the $GABA_A$ α4 Subunit Leads to Increased Airway Resistance and Inflammation," and Creed Stary, M.D., Ph.D., of Stanford University for his talk entitled, "miR-200c Contributes to Injury from Transient Cerebral Ischemia in Mice by Targeting Reelin." Each year the SAB also recognizes two outstanding poster discussion presentations. Andrew Hudson, M.D., Ph.D., from UCLA was recognized for his presentation of "A Network of Discrete Metastable Activity States Mediates Recovery from Isoflurane Anesthesia." The second best poster discussion presentation was awarded to Randolph Hastings, M.D., Ph.D., of the VA San Diego Healthcare System for "Training Factors that Modulate Laryngoscopy Learning." The scientific program of the AUA is the product of the Scientific Advisory Board which thanks three members rotating off the SAB after 3 years of service, Max Kelz, M.D., Ph.D.; Dean Andropoulos, M.D., and Dolores Njoku M.D., and welcomed three new members, Y.S. Prakash, M.D., Ph.D., Matthias Ludwig Riess, M.D., Ph.D., and Wei Chao, M.D., Ph.D. The SAB looks forward to an exciting scientific program next year at Vanderbilt University in Nashville, Tennessee.

The inaugural Margaret Wood Resident Research Award, established to inspire and recognize original resident research was awarded to Katie Schenning, M.D., M.P.H., from Oregon Health and Science University for her talk entitled, "Postoperative Dementia: Role of Anesthesia and APOE4."



Abstract authors presented their research during two moderated poster discussion sessions.

Dr. Terrando was one of the abstract award winners who presented his research during two of the oral sessions.

Report on SAB Plenary Panel: Lung Injury, Remodeling and Repair

Marek Brzezinski, M.D., Ph.D.
Associate Professor
University of California – San Francisco

Let's start by stating that the 2 hours of this panel were perhaps some of the best an AUA Annual Meeting has offered: educational, exciting, and inspirational – a benchmark for future panels.

Sponsored by the American Journal of Physiology-Lung Cellular and Molecular Physiology, this symposium was organized by Drs. Charles Emala (Vice Chair for Research, Columbia University), Y. S. Prakas (Vice Chair for Research, Mayo Clinic), and Sadis Matalon (Editor in Chief of AJP-Lung, Vice Chair for Research, University of Alabama at Birmingham) who also moderated the session.

The session started with the keynote speaker Dr. Charles N. Serhan, the Simon Gelman Professor of Anesthesia at Brigham and Women's Hospital. Dr. Serhan gave a truly innovative and visionary presentation, entitled *"Novel Pro-Resolving Mediators & Mechanisms on Inflammation: Immunoresolvents,"* focusing on recent advances by his lab on lipid-derived mediators that play a key role in endogenous anti-inflammation and its resolution. His work changed the >100-year-old concept that the resolution of inflammation is a passive process. Dr. Charles Serhan started by introducing the novel families of potent bioactive lipid-derived mediators, coined resolvins and protectins, that his group recently discovered. Each of these pro-resolving mediators controls the duration and magnitude of acute inflammation in vivo with stereospecific actions in the pico- to nanogram range. These new families of local chemical mediators were originally identified in murine exudates captured during the natural self-limited phase. The specialized pro-resolving mediators (SPM) include 3 distinct chemical mediator families he named resolvins, protectins, and the most recent addition, maresins. These are biosynthesized from essential omega-3 fatty acids (EPA and DHA) and possess potent multi-pronged anti-inflammatory, pro-resolving, and anti-microbial actions in models of sepsis and in pain. Dr. Serhan pointed out that his group found the actions of SPM to be potent, cell type-specific, and stereoselective with human cells and in experimental animal diseases. In mice, 12/15-LOX expression protects from atherosclerosis via local production of SPM including lipoxin A_4, resolvin D1, and protectin D1. He went on to say that the endogenous formation of resolvins and protectins and their protective roles were recently confirmed and extended in other models, including murine ischemic renal injury and obesity-induced insulin resistance and liver disease. His group established the complete stereochemistry of each of the resolvins and protectins. He then focused on the resolvins coined Resolvin D3 (RvD3) and its aspirin-triggered 17*R*-epimer (AT-RvD3), as both display potent actions in mouse inflammation and with human leukocytes (neutrophils and macrophages).

Dr. Serhan concluded his talk by summarizing that 1) Identification of endogenous SPM biosynthesized during inflammation-resolution in diverse animal models and recently in human serum and plasma indicates that the resolution of acute inflammation is an active programmed process. 2) This work changed the >100-year-old concept that the *resolution of inflammation is a passive process.* 3) Together these findings indicate that endogenous resolution pathways may underlie many prevalent diseases associated with uncontrolled inflammation and open the potential for resolution-based pharmacology.

The next speaker was Dr. Brant Wagener, a FAER fellow mentored by Drs. Pittet and Matalon from the University of Alabama at Birmingham, with a talk entitled, *"IL-8 and cAMP-stimulated Alveolar Epithelial Fluid Transport in Acute Lung Injury: Why did the Multicenter NIH/ARDS Network and BALTI-2 Trials with β2- adrenergic agonists fail?"* Dr. Wagener gave a passionate presentation on why single-agent therapy with beta-agonists may have failed in patients with ARDS and introduced a novel strategy to enhance the effectiveness of beta-agonist therapy. This first presentation by Dr. Wagener in a major scientific meeting was supplemented by a good sense of humor that made his talk very enjoyable. His data suggest that the single agent therapy for the treatment of acute respiratory distress syndrome (ARDS) with β2-agonists may have failed due to the fact that chemokines released during the inflammatory response (e.g., IL-8) heterologously desensitize the β2-AR via a PI3K- and GRK2-dependent mechanism. Thus, the β2-AR is inactivated BEFORE it can be bound by β2-agonists therefore significantly decreasing cAMP-mediated alveolar fluid clearance. He moved on to show data demonstrating that IL-8's inhibitory effect on the β2-AR can be reversed by inhibitors of PI3K that allow recovery of increased alveolar fluid clearance in response to low-dose β2-agonists. This process of reversal may allow clinicians to accelerate alveolar fluid clearance in patients with ARDS and decrease the mortality and/or morbidity from this disease process. He concluded his talk by pointing out that future work needs to 1) focus on mechanisms by which inflammatory mediators inhibit β2-AR function in the lung, and 2) identify mechanisms and chemotherapeutic agents that reverse IL-8's inhibitory effect.

The third panel speaker was Dr. Jae Woo Lee from University of California, San Francisco. His presentation, entitled *"Cell-Based Therapy for Acute Lung Injury,"* provided an update on the biological rationale for the on-going Phase I/II clinical trial looking at the therapeutic effects of bone marrow-derived mesenchymal stem cells (MSC) in patients with ARDS. Dr. Lee started by pointing out that ARDS remains a major cause of morbidity and mortality in hospitalized patients, potentially due to the failure of translating experimental pharmacologic therapies into effective clinical treatment options. With this

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Report on SAB Plenary Panel

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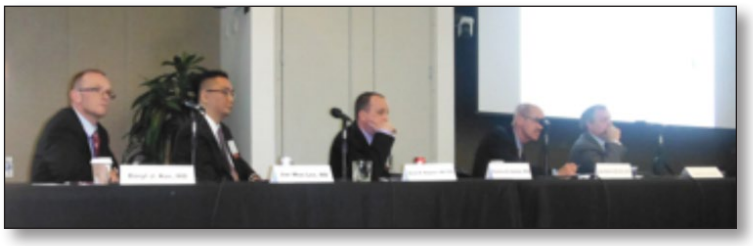
"Each of these pro-resolving mediators controls the duration and magnitude of acute inflammation in vivo with stereospecific actions in the pico- to nanogram range."

introduction Dr. Lee made the case for new and innovative therapies focused on mesenchymal stem cells: Adult stem cells, specifically bone marrow-derived mesenchymal stem or stromal cells (MSC), have been shown to be therapeutic in various small animal models of acute lung injury primarily due to the capacity of MSC to secrete multiple paracrine factors that can regulate lung endothelial and epithelial permeability, enhance pulmonary edema resolution and tissue repair, decrease inflammation, and inhibit bacterial growth. In the *ex vivo* perfused human lung model of pneumonia, his group was able to demonstrate that the administration of MSC had effects additive to the addition of antibiotics in reducing the total bacterial load and the inflammatory milieu of the injured lung. He then provided a brief update on the on-going Phase I/II clinical trial (NCT02097641, PI Michael Matthay) that looks at the therapeutic effects of bone marrow-derived MSC in patients with ARDS. Dr. Lee concluded his talk by pointing out that although the MSC therapy is promising, future research is needed to determine the optimal dose and route of MSC administration as well as the development of a potency assay to better compare different adult stem cells as therapy.

The fourth and final speaker was Dr. Daryl J. Kor from Mayo Clinic with a presentation, entitled *"Platelet function and ARDS pathogenesis: A path to prevention?"* Dr. Kor started his very well presented talk by pointing out that ARDS is a leading cause of postoperative respiratory failure. He then went on to identify two major barriers to progress in this regard: an incomplete understanding of the mechanisms underlying ARDS and an inability to identify patients at risk. With this background, Dr. Kor focused his talk on the increasing evidence supporting a critical role for platelets, platelet-neutrophil interactions, and platelet-derived anti-inflammatory lipid mediators in the development and resolution of ARDS. He reviewed the growing body of subclinical and observational data supporting the notion that antiplatelet therapies such as aspirin (ASA) may have a role in mitigating the development and progression of ARDS, highlighting the groundbreaking work of his group that identified an independent association between ASA therapy and decreased development of ARDS in three large cohorts of at-risk patients. He concluded his talk by updating the audience on the ongoing large multicenter phase II trial evaluating the role of ASA as an ARDS prevention strategy to further define these associations. His team is also investigating the potential value of platelet-derived biomarkers in refining our ability to identify patient cohorts who are at greatest risk of developing ARDS.



The *American Journal of Physiology – Lung Cellular and Molecular Physiology* sponsored the SAB Plenary Panel: "Lung Injury, Remodeling and Repair."

Overall, the main learning points of this panel were:

1. Resolution of inflammation is an active process and opens the potential for resolution-based pharmacology.
2. Single-agent therapy with beta-agonists doesn't work in ARDS.
3. Mesenchymal stem cell-based therapy in ARDS has provided promising results in pre-clinical studies and is now being examined in human studies.
4. Aspirin, its use potentially going as far back as the time of Hippocrates, continues to amaze – growing evidence suggests that it possibly can even prevent ARDS.

In summary, there is no substitute for coming to AUA meetings.

ASA President's Update at 2014 AUA Annual Meeting

Alex Macario, M.D., M.B.A.
Stanford University

Dr. Jane Fitch, ASA President, and Professor and Chair of the Department of Anesthesiology at the University of Oklahoma, gave the ASA President's Update. The focus of her presentation was on how to get things done at ASA. She highlighted the fact that a majority of the elected positions in the ASA are currently held by academic anesthesiologists. Dr. Fitch also presented the ASA organizational diagram to describe who reports to who and the multiple channels available to anesthesiologists to be involved. She updated the group on a variety of issues including ASA's work to halt the application of the Veterans Health Administration Nursing Handbook to replace care "provided in a team fashion" with a requirement that all Advanced Practice Registered Nurses (APRN), including nurse anesthetists, "attain independent status."

Host Program Summary 2014 AUA Annual Meeting

Alex Macario, M.D., M.B.A.
Stanford University

The Stanford Host Program, arranged by Dr. Ron Pearl on the morning of Saturday April 26, 2014, had four outstanding speakers with entertaining presentations covering a wide range of topics.

David M. Kennedy, Ph.D. (Pulitzer Prize winner in 2000), Professor Emeritus at Stanford specializing in American history, got the ball rolling with "Who Bleeds? Who Pays? Rethinking the Modern American Military." His presentation described the effect of the United States eliminating the draft in 1973 and moving to an all-volunteer force. According to

> *"As a result, the broader society currently has less 'skin in the game' when the country is at war."*

Professor Kennedy, this resulted in a military that is not broadly representative of American society. Specifically, many recruits come from disadvantaged communities primarily from families in the middle or lower middle classes such that when there are military interventions abroad the impact and disruption on civil society is much less than prior to the Vietnam War. This is even more the case now because the military is a much smaller fraction of the economic activity of the entire country as compared to the period after World War II. As a result, the broader society currently has less "skin in the game" when the country is at war.

The second talk was by Dr. Sam Gambhir, Chair, Department of Radiology, at Stanford and titled, "Recent Advances in Multi-Modality Molecular Imaging." The challenge is to image the human body for things that are less than one millimeter in size. This includes for example tiny tumors. He described the magneto-nanosensor chip technology developed at Stanford for blood-based diagnostic or prognostic protein biomarkers requiring very small sample volumes. Other ongoing research and futuristic applications of imaging assays to monitor cellular and molecular events were highlighted, including development of novel tracers (e.g., Photoacoustics) for early cancer detection.

The session's next exciting talk, "The Secret Life of Elephants," was given by Caitlin E. O'Connell- Rodwell, Ph.D., Assistant Professor, Department of Otolaryngology, Head & Neck Surgery at Stanford. Elephants communicate via low frequency vocalizations that are not only heard but also detected by the elephants as vibrations in the ground. These acoustic and seismic signals allow elephants to estimate the distance

David M. Kennedy, Ph.D., presented "Who Bleeds? Who Pays? Rethinking the Modern American Military."

at which the signal is coming, helping with localization of the sound. As a result of these studies and findings, the speaker has helped the Namibian government work with farmers struggling to deter wild elephants destroying crops by creating sound deterrents. Her work may also lead to innovative listening devices for patients with hearing impairment.

To conclude, John L. Hennessy, Ph.D., Stanford University President for more than a decade, was the fourth speaker of the morning. Hennessy articulated the crucial elements of the "Silicon Valley and the Role of Stanford University" in creating the entrepreneurship ecosystem that exists in the San Francisco Bay Area. It may be difficult for other communities here in the USA or abroad to recreate this academic research environment which has a longer time horizon for return on investment than industry can afford. This also depends on young people, often students, taking risky projects (in a supportive culture) that often fail but when succeed, change the world. Recent examples include Google and Yahoo, and before that Cisco and before that Hewlett Packard.

Call for Host Applications for the AUA 63rd Annual Meeting in San Francisco

The Association of University Anesthesiologists is requesting applications from the membership to host the AUA 63rd Annual Meeting, May 19-21, 2016, in San Francisco, California.

The AUA will continue the tradition of the Host Program in 2016. The Host Institution can come from anywhere in the country and may present the topics that exemplify the spirit, breadth and depth of their institution. For more information on the Host Program tradition, check out AUA President Dr. Thomas J.J. Blanck's message on the AUA website at **auahq.org/presidents-message**.

Host Applications should include a detailed description of the proposed program and potential speakers. The Host Program will likely be presented on Friday morning May 20, 2016, from 8:00 am to 11:00 am. The Host Institution will be responsible for the cost of the travel and accommodations of their speakers.

The deadline to submit host applications for the 2016 Annual Meeting is **August 31, 2014**. The applications will be reviewed by the AUA Council during their meeting at 2014 ASA Annual Meeting in New Orleans. The 2016 Host Institution will be chosen by the Council at that time and notified shortly following the meeting.

Please submit applications to Meghan Whitbeck, AUA Meetings Manager, in Word or PDF format at: **auameetings@iars.org.**

Meet this Year's AUA Council

The Association of University Anesthesiologists membership elected a President-Elect, Secretary and one Councilor-at-Large to the AUA Council for the upcoming year at the AUA Annual Business Meeting on April 25, 2014 at the AUA 61st Annual Meeting in Stanford, California. Check out the current AUA Council Roster below.

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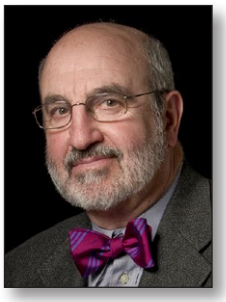
New York University
School of Medicine



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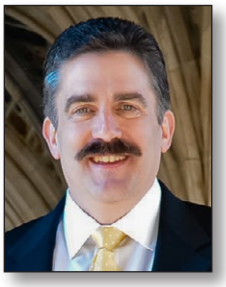

Robert Pearce, M.D., Ph.D.
University of Wisconsin School of Medicine and Public Health in Madison

Congratulations to the New AUA Members for 2014!

The following individuals were elected to active membership status at the AUA Annual Business Meeting on April 25, 2014 at the AUA 61st Annual Meeting in Stanford, California. They bring a wealth of experience in a wide range of areas that will add to the membership base. Look forward to meeting them at the AUA 62nd Annual Meeting, April 23-25, 2015, in Nashville, Tennessee!

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FAER Commits over $2.5M to Research Funding

Denham S. Ward, M.D., Ph.D.
President, FAER
University of Rochester Medical Center

Each Spring, the FAER Board of Directors meets prior to the AUA meeting. A primary goal of this meeting is to determine the eligibility and funding level for grants submitted in the current cycle. The table below shows the number of applications received and the percent that FAER funded. This year FAER committed to over $2.5M in research grant funding. Funded grants ranged from those for medical student research up through education research grants available to senior faculty. FAER's funding was supplemented by the AQI for the Health Services Research grants and by departments hosting medical students for the summer research. These, combined with substantial research grant funding independently provided by the IARS and the subspecialty societies, show remarkable support for research within the specialty.

In 2014, FAER expanded the research opportunities offered by the Medical Student Anesthesia Research Fellowship program from the Summer fellowship to include a year-long fellowship. The MSARF Year-Long grant provides a student stipend, as well as funds for other expenses, that enable a student to work on a research project while taking a year's leave from their medical studies. In this inaugural year for the year-long grant, FAER received five applications. Of these five, two were funded: Rebecca Bickham, BS will do research on "Predicting postoperative opioid-related adverse events and unplanned admissions in children with sleep-disordered breathing" at the University of Michigan, and Claudia Sotillo, BS will do research on "Next Generation Sequencing: an approach to identify genetic susceptibility for rheumatic heart disease" at Brigham and Women's Hospital. If you know a third or fourth-year medical student passionate about research, encourage them to investigate FAER's MSARF Year-Long grant.

Overall, FAER's funding rate continues to be above 30% - great odds considering the current NIH "payline." However, only one Research Fellowship Grant application was submitted this year. With the rise in residents doing single-year clinical fellowships, a corresponding rise in RFG applications might have been anticipated. Also, the funding rate for clinical-translational research lags behind that of basic science research and health services research. Many of the clinical-translational research proposals would have benefited from more detailed mentoring and career development plans as well as data showing the feasibility of the proposed study. Other areas in which AUA members can play a key role are 1) promoting the availability of the Research Fellowship Grants and 2) working with promising residents in your department to enhance the quality of grant applications. With your help, an increase in application quality and funding could be dramatic.

More information about FAER's grants and the grant recipients can be found at **FAER.org/research-grants**. These grants are made possible by the generous donations from the ASA, the AUA and other societies. Individual donations are also a vital part of our revenue. Please consider donating to FAER: **FAER.org/donate**.

Grant	Applications	Institutions	% Funded
MRTG-BS	15	14	53%
Clinical Research	19	13	26%
MRTG-CT	13	9	15%
MRTG-HSR	6	6	50%
REG	6	5	33%
RFG	1	1	100%
Medical Students	146	74	43%
MSARF - summer	141	74	43%
MSARF - year long	5	5	40%

Table 1 FAER grant funding for 2014. MSARF – Medical Student Research Fellowship. MRTG – Mentored Research Training Grant in basic science (BS), clinical translational (CT) or health services research (HSR). REG - Research in Education Grant. RFG – Research Fellowship Grant.

Check Out the New AUA Website

Learn more about the association, its role in advancing anesthesiology with the easier navigation system.

Access the updated Members-Only Portal and find the information you need.

Visit the AUA website at **auahq.org**.

Update on Obstetric Anesthesia

SOAP Society for Obstetric Anesthesia and Perinatology

Robert Gaiser, M.D., President, Society for Obstetric Anesthesia and Critical Care University of Pennsylvania

Current obstetric practice is different from the management – plus most were trained as a resident or fellow. While the placement of an epidural catheter in a laboring patient remains the mainstay of the obstetric anesthesiologist, its management continues to be refined.

The major change in the provision of epidural labor analgesia is the use of low local anesthetic concentrations.[1] The limits to the lowest possible concentration are currently being established but the theme remains the same: the addition of an opioid to the local anesthetic will allow for a synergistic effect and for a decrease in the concentration of the local anesthetic. The advantage to the lower concentration is the lesser degree of motor blockade in the mother, with some anesthesiologists permitting the patient to walk following a bolus.[2] The well-established advantage to the lower concentrations is the reduced incidence of operative vaginal delivery.[3] While the decrease in forcep-assisted vaginal delivery has been attributed to the greater risk of malpractice claims, it also may be due to the fact that the use of lower concentrations of local anesthetic through the epidural catheter.

Currently, the dosing of the epidural catheter for the management of labor pain is a continuous infusion with the possibility of the mother administering additional boluses by pressing a button. Patient controlled epidural analgesia has been advocated as it increases maternal satisfaction with her analgesia and also decreases the amount of local anesthetic used as compared to intermittent boluses during a continuous infusion based upon maternal request.[4] Mothers frequently request boluses as she transitions to the second stage. A continuous infusion will maintain a level of analgesia that would not be sufficient for the second stage of labor which involves the pudendal nerve; the pudendal nerve is derived from the S2-S4 spinal nerves. One approach to manage this situation would be the administration of programmed intermittent boluses as compared to a continuous infusion. One hundred and ninety women were randomized to one of three programmed infusion regimens.[5] The local anesthetic that was administered through the epidural catheter was 0.0625% bupivacaine with fentanyl 1.95 µg/mL. Group 1 received 2.5 mL every 15 minutes (very close to a continuous infusion); Group 2 received 5 mL every 30 minutes; Group 3 received 10 mL every 60 minutes. Patients were allowed to receive additional boluses of local anesthetic upon request. Given the ability to bolus upon request, there was no difference in patient satisfaction; however, there was less use of local anesthetic in Group 3. Those patients who received the larger bolus less frequently required top-up boluses. This study suggests that a programmed intermittent bolus will provide better labor analgesia. The result of this study was confirmed in a meta-analysis of nine trials of 345 patients.[6] The intermittent bolus technique did reduce local anesthetic use and improved maternal satisfaction. The technique was limited by the availability of pumps able to deliver intermittent boluses. This limitation no longer exists and most hospitals will most likely be transitioning to the intermittent bolus technique.

Another change in the provision of analgesia for laboring patients is the increased use of patient-controlled analgesia using opioids. Traditional PCA consisted of morphine and fentanyl. The use of fentanyl for the management of labor analgesia has been well described and typically consists of a 50-100 µg bolus with the ability to administer 50 µg every 10 minutes.[7] With this technique, there is a high incidence of maternal sedation and naloxone use in the neonate. The use of remifentanil for labor analgesia has recently been investigated.[8] Remifentanil has the advantage of rapid metabolism; although it crosses the placenta to a great extent, it is rapidly metabolized by non-specific esters in the fetus and neonate. Forty laboring parturients were randomized to receive either epidural analgesia of 0.1% bupivacaine with fentanyl 2 µg/cc or to intravenous remifentanil starting at 0.02 mg with the ability to increase the bolus up to 0.06 mg with a lockout interval of 1 to 2 minutes. While epidural analgesia provided better analgesia than remifentanil (avg VAS-pain 3.7 vs 1.5), remifentanil did decrease the VAS-pain from an average of 8.4 to 3.7. Five women in the remifentanil group developed apnea events and had lower mean oxygen saturation with no difference in neonatal respiratory events from the epidural group. While many may consider the use of remifentanil for labor analgesia in individuals in whom epidural analgesia is contraindicated, the increased cost for the drug and for the time involved may render it less ideal than fentanyl. In a randomized study of PCA fentanyl and remifentanil, remifentanil provided better satisfaction scores with a difference in VAS-pain for the first hour only.[9] As such, both remifentanil and fentanyl are options for analgesia when epidural analgesia is contraindicated.

The use of neuraxial anesthesia for cesarean delivery continues to increase. The use of general anesthesia is reserved for the parturient in whom there is insufficient time or in whom the epidural catheter is non-functional. The incidence of failed intubation during general anesthesia has been studied. The first report was by Rocke et al, who reported that difficult intubation was associated with a greater Mallampati score, short neck, and receding mandible.[10] In a large series of 49,500 deliveries in Australia in 2005, 1095 parturients required general anesthesia. Of these patients, four experienced a failed intubation resulting in an incidence of 1:274.[11] However, these results are from a time period when videolaryngoscopy may not have been available. The UK Obstetric Surveillance System reviewed 57 cases of failed intubation from 2008 to 2010.[12] The incidence of failed intubation was 1:224 (essentially not much different). From the study it was not possible to determine whether videolaryngoscopes were available. Risk factors

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Update on Obstetric Anesthesia

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for difficult intubation included increases in age, weight, and Mallampati score. The full impact of the availability of videolaryngoscopy has not been determined. An extremely small series demonstrated that the failed direct laryngoscopy was rescued with videolaryngoscopy.[13]

A major change in the provision of general anesthesia for cesarean delivery occurred with the publication by Ueyama, et al.[14] General anesthesia for cesarean delivery has a high incidence of awareness. This increased incidence was attributed to the management of the anesthetic with the thought providers avoided the use of agents to prevent an effect on the fetus and providers decreased the concentration of inhaled anesthetic because MAC was decreased by 30% in pregnancy. MAC appears to be a spinal reflex and does not reflect the brain. Rather than relying on movement to surgical stimulus, Ueyama et al examined 15 patients undergoing cesarean delivery and 15 patients undergoing elective gynecologic surgery as to the effect of sevoflurane on electroencephalographic signals. There was no difference in the amount of anesthetic required to affect the electroencephalographic signals. As such, the anesthetic requirements for pregnant patients were not decreased. This study has resulted in a change in the management of general anesthesia for cesarean delivery as providers must provide the same amounts of anesthesia as they would provide to a nonpregnant individual.

In regard to neuraxial anesthesia for cesarean delivery, the overwhelming majority of patients receive preservative free morphine for postoperative analgesia. In a dose response study, the dose for intrathecal morphine for women receiving spinal anesthesia for cesarean delivery is 0.1-0.2 mg, while for epidural anesthesia it is 3-4 mg. The specialty has experienced drug shortages which has affected practice. One drug shortage was for preservative free morphine. Providers were confronted with the challenge of providing effective postoperative analgesia without the drug. The transverses abdominis plane block became a viable alternative. The TAP block involves injecting approximately 20 mL of local anesthetic between the internal oblique and the transverses abdominis muscles. Given its effectiveness, the TAP block was compared to neuraxial morphine; neuraxial morphine provided improved analgesia with the addition of a TAP block not improving the analgesia. As such, the TAP block serves as an alternative if neuraxial opioids are not used or if the procedure was performed during general anesthesia.[15]

Finally, one major change in the administration of neuraxial anesthesia for the parturient is the management of hypotension. Previously, ephedrine was used as it felt to maintain uterine blood flow to a better extent than phenylephrine. This observation was based upon an animal model. Subsequent studies demonstrated that umbilical cord pH (one of the factors that reflects uterine blood flow) was higher in parturients who received phenylephrine as compared to ephedrine for the treatment of the hypotension. Further studies have demonstrated that the difference in umbical cord pH is not due to a difference in uterine blood flow, rather to ephedrine crossing the placenta to a greater extent stimulating the release of fetal catecholamines.[16] As such, most use phenylephrine for the management of hypotension during cesarean delivery. The addition of a continuous infusion of phenylephrine will have no difference in umbilical cord pH as compared to intermittent boluses. The continuous infusion will result in a lower incidence of nausea and vomiting as compared to intermittent boluses.[17]

The provision of anesthesia for the patient undergoing delivery has evolved from a dense epidural analgesic with ephedrine for the treatment of hypotension. These changes are the result of the tireless efforts of the physician scientists who continually strive to improve care of the parturient.

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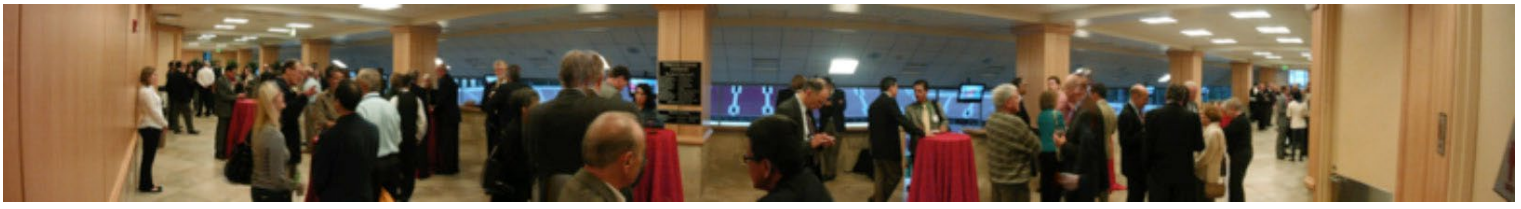
AUA 61st Annual Meeting in Pictures

More photos from the AUA 61st Annual Meeting here.



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